REMARKS

Claims 1-37 are pending. Claim 22 was objected to. Claims 1-33 were rejected under 35 U.S.C. §112, second paragraph. Claims 2 and 9-12 were rejected under 35 U.S.C. §112, first paragraph. Claims 1-4, 6-8, 13, 14, 17, 20-36 were rejected under 35 U.S.C. §102(a). Claims 1-4, 6-8, 13-15, 17 and 20-36 were rejected under 35 U.S.C. §102(b). Claims 5, 15, 16, 18-19, and 37 were variously rejected under 35 U.S.C. §103(a).

By this amendment, claims 2, 3, 7-10, 24 and 34-36 have been canceled, claims 1, 4-6, 11, 12, 22, 25, 26 and 37 have been amended and new claims 38-52 have been added herein without prejudice or disclaimer of any previously claimed subject matter.

Support for the amendments and new claims can be found throughout the specification. For example, support for the amendment to claim 1 is found, *inter alia*, on page 6, lines 27-29 and lines 30-31. Support for the amendment to claims 11 and 12 is found, *inter alia*, on page 15, lines 19-25. Support for the amendment to claim 22 is found, *inter alia*, on page 6, lines 17-18. Support for new claim 40 is found, *inter alia*, on page 21, lines 28-31. Support for new claim 43 is found, *inter alia*, on page 8, lines 2-7. Support for new claim 45 is found, *inter alia*, on page 8, lines 7-10. Support for new claims 41, 42 and 44 is found, *inter alia*, on page 22, line 12. Support for new claims 38 and 47 is found, *inter alia*, on page 49, line 17-20. Support for new claims 39 and 48 is found, *inter alia*, in originally filed claim 16. Support for new claims 46, 49, 50, 51 and 52 is found, *inter alia*, in originally filed claims 14, 17, 18, 19 and 20, respectively.

The amendments are made solely to promote prosecution without prejudice or disclaimer of any previously claimed subject matter. With respect to all amendments and canceled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover has not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Interview

Applicants' representative wishes to thank Examiners Foley, Parkin and Scheiner for extending the courtesy on an interview to Applicant and Applicants' representative and providing helpful suggestions on October 3, 2001. The amendments and remarks reflect discussion and suggestions made during the interview.

Applicants have carefully considered the points raised in the Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Claim objection

Claim 22 was objected to because of an alleged informality. Applicants respectfully traverse this objection. Claim 22 is recites that "production of second antigen-specific Th1-associated antibodies is stimulated" (emphasis added). Thus, the claim is grammatically correct. Accordingly, Applicants respectfully request that the objection be withdrawn.

Rejections under 35 U.S.C. §112, second paragraph

Claims 1-33 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants respectfully traverse this rejection.

Although Applicants believe that the claims were sufficiently definite when considered in view of the specification and the understanding of those of skill in the art, Applicants have attempted to respond to each of the various comments by the Examiner to facilitate disposition of the present case.

With regard to claim 1, the Examiner questioned how it can "be determined that exposure to the first antigen will elicit an immune response to a second antigen if the second antigen is never encountered." Office Action, page 2. As discussed in the interview, it is evident from the

language of claim 1 before amendment that the composition is administered in an amount sufficient to modulate an immune response to the second antigen upon exposure to the second antigen. Thus, the claim is not directed to a situation where the second antigen is never encountered.

However, claim 1 and, accordingly all claims dependent from claim 1, including claims 11 and 12, have been amended to recite administering a second antigen with the immunomodulatory polynucleotide and first antigen. The Examiner indicated during the interview that this amendment would be acceptable and overcome this rejection. Claims 2 and 8-10 have been cancelled.

With regard to claim 5, the specification provides descriptions and examples of platform molecules, for example, at page 33, line 28, to page 34, line 28. Thus, Applicants submit that what is intended by a "platform molecule" is not indefinite and the invention of claim 5 is distinctly claimed.

Accordingly, in view of the amendments and remarks herein, Applicants respectfully request that the rejection of claims under 35 U.S.C. §112, second paragraph, be withdrawn.

Rejections under 35 U.S.C. §112, first paragraph

Claims 2 and 9-12 were rejected under 35 U.S.C. §112, first paragraph, because the specification allegedly does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. Applicants respectfully traverse this ground for rejection.

The Examiner admits that the specification is enabled for "encountering a second pathogen at a specific time and place upon administration" but asserts that the specification does not "reasonably provide enablement for encountering a second pathogen at a specific time and place where it is encountered in the environment." The Examiner further asserts that there "is no

way to predict exactly where or when exposure to an antigen will occur in the environment." Office Action, page 4.

Applicants respectfully disagree with these assertions. Situations certainly exist when and/or where one can reasonably anticipate exposure to an antigen. In the context of allergies, for example, one can anticipate exposure to a plant allergen during its particular allergy season or exposure to animal dander allergens upon encounter with a pet animal. In the context of infectious disease, one can anticipate exposure to influenza antigens during flu season and/or when in the presence of someone infected with influenza or one can anticipate exposure to antigens of sexually transmitted pathogens through association with infected individuals with opportunities for exposure (*e.g.*, spouses, partners, prostitutes, etc.). Thus, Applicants submit that there are many examples of situations when one can anticipate a time and/or place of environmental exposure to antigens.

Nevertheless, as discussed in the interview, and in the interest of expediting prosecution, claims 2, 9 and 10 have been canceled and the remaining claims have been amended to recite administering (i) an immunomodulatory polynucleotide proximately associated a first antigen with (ii) a second antigen. Applicants submit that the pending claims are enabled and accordingly, respectfully request that the rejection of claims under 35 U.S.C. §112, first paragraph, be withdrawn.

Rejections under 35 U.S.C. §102

Claims 1-4, 6-8, 13, 14, 17, 20-36 were rejected under 35 U.S.C. §102(a) as allegedly being anticipated by Schwartz et al. (WO 98/55495, "Schwartz"). Applicants respectfully traverse this ground for rejection.

Schwartz describes the use of immunostimulatory oligonucleotide and antigen compositions to modulate an immune response to the antigen (*i.e.*, the antigen which is proximately associated with the immunostimulatory polynucleotide). However, with regard to

the claims before amendment, Schwartz does not disclose modulation of an immune response to a second antigen based on administration of a first antigen linked to an immunomodulatory polynucleotide and exposure to a second antigen. With regard to the claims as amended, Schwartz does not describe the claimed invention, *i.e.*, administration of (i) an immunomodulatory polynucleotide proximately associated with a first antigen with (ii) a second antigen, where the amount of the polynucleotide and first antigen administered is sufficient to modulate an immune response to the second antigen.

As it does not teach modulation of an immune response to a second antigen through administration of the second antigen with an immunomodulatory polynucleotide proximately associated with a first antigen, Schwartz does not anticipate the claimed invention.

Claims 1-4, 6-8, 13, 14, 17, and 20-36 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Carson et al. (WO 98/16247, "Carson"). Applicants respectfully traverse this ground for rejection.

Carson describes the use of immunostimulatory polynucleotides linked to an antigen to modulate an immune response to the antigen (*i.e.*, the antigen which is linked to the immunostimulatory polynucleotide). With regard to the claims before amendment, Carson does not disclose modulation of an immune response to a second antigen based on administration of a first antigen linked to an immunomodulatory polynucleotide and exposure to a second antigen. With regard to the claims as amended, Carson does not describe administration of (i) an immunomodulatory polynucleotide proximately associated with a first antigen with (ii) a second antigen, where the amount of the polynucleotide and first antigen administered is sufficient to modulate an immune response to the second antigen.

As it does not teach modulation of an immune response to a second antigen through administration of the second antigen with an immunomodulatory polynucleotide proximately associated with a first antigen, Carson does not anticipate the claimed invention.

In sum, the cited references do not teach or suggest every element of the pending claims, thus neither Schwartz nor Carson can anticipate the present invention. Accordingly, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §102(a) and §102(b).

Rejections under 35 U.S.C. §103

Claims 5, 15, 16, 18, 19 and 37 were variously rejected under 35 U.S.C. §103(a) as follows. Claim 5 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Schwartz or Carson as applied to claims 1-4, 6-8, 13, 14, 17, 20-36 above, and further in view of Rose (1998, *J. Ther. Biol.* 195:111-128). Claim 15 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Schwartz or Carson and Rose as applied to claims 1-8, 13, 14, 17, 20-36 above, and further in view of Lee et al. (1998, *Ann Med.* 30:460-468, "Lee"). Claim 16 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Schwartz or Carson, and Rose, as applied to claims 1-8, 13, 14, 17, 20-36 above, and further in view of Durali et al. (1998, *J. Virol.* 72:3547-3553, "Durali"). Claims 18 and 19 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Schwartz or Carson, Rose, Lee and Durali as applied to claims 1-8, 13-17, 20-36 above, and further in view of Anderson (U.S. Patent No. 4,673,574). Claim 37 stands rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Schwartz or Carson, Rose, Lee, and Durali and Anderson as applied to claims 1-8 and 13-36 above.

Applicants traverse these rejections and respectfully point out that the cited references do not support *prima facie* obviousness with regard to the claimed invention.

The claimed invention (as amended) is directed to methods of modulating an immune response to a second antigen through administration of (i) an immunomodulatory polynucleotide proximately associated with a first antigen with (ii) a second antigen, where the amount of the polynucleotide and first antigen administered is sufficient to modulate an immune response to

the second antigen. Claim 5 is directed to the method where the polynucleotide and first antigen are proximately associated by a platform molecule. Claims 15 and 16 are directed to methods where the first antigen is influenza nucleocapsid protein and HIV gag protein, respectively. Claims 18 and 19 are directed to methods where the first antigen is CRM 197 and diphtheria toxoid, respectively. Claim 37 is directed to a composition comprising (i) an immunomodulatory polynucleotide proximately associated with a viral conserved polypeptide and (ii) a viral variable polypeptide.

To establish a prima facie case of obviousness, the combined references must teach or suggest all the claim limitations. *In re Royka*, 180 USPQ 580 (CCPA) 1974.

As outlined above, neither Schwartz nor Carson teach or suggest the rejected claims nor teach or suggest the claims as amended. With regard to the claims as amended, neither Schwartz or Carson describe administration of (i) an immunomodulatory polynucleotide proximately associated with a first antigen with (ii) a second antigen, where the amount of the polynucleotide and first antigen administered is sufficient to modulate an immune response to the second antigen.

The secondary reference Rose describes platform molecules and the use of platform molecules to link various agents in the treatment of cancer. Lee describes the use of DNA vaccines encoding influenza proteins in tests for infection protection. Durali describes production of cytotoxic T lymphocytes against HIV antigens from various HIV clades. Anderson describes diphtheria toxoid and diphtheria CRM 197 as carriers in vaccine preparations.

The secondary references do not supply what is missing from the primary reference, Schwartz or Carson, and the combinations of Schwartz or Carson and the secondary references do not teach or suggest the claimed invention, thus do not render the claimed invention obvious.

One element that distinguishes the claimed invention from the cited references is the use of an immunomodulatory polynucleotide proximately associated with a first antigen to modulate

an immune response to a second antigen. In the present invention, an immunomodulatory polynucleotide proximately associated with a first antigen is administered with a second antigen in an amount sufficient to modulate an immune response to the second antigen. None of the references, either alone or in combination, describes or suggests modulation of an immune response to a second antigen through administration of the second antigen with an immunomodulatory polynucleotide proximately associated with a first antigen. Also, none of the references, either alone or in combination, describes or suggests a composition as claimed.

Further, Applicants submit that there in no suggestion in the art or in these references to modify their teachings to arrive at the claimed invention.

Accordingly, Applicants respectfully submit that Examiner has failed to establish a *prima facie* case of obviousness and respectfully request withdrawal of the rejections under 35 U.S.C. §103.

CONCLUSION

Applicants believe that all issues raised in the Office Action have been properly addressed in this response. Accordingly, reconsideration and allowance of the pending claims is respectfully requested. If the Examiner feels that a telephone interview would serve to facilitate resolution of any outstanding issues, she is encouraged to contact Applicants' representative at the telephone number below.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is entitled "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**".

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for

any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 377882000800. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: January 30, 2002

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please enter the following amendments without prejudice or disclaimer.

In the Claims:

Please amend claims 1, 4-6, 11, 12, 22, 25, 26 and 37 as follows.

1. (Amended) A method of modulating an immune response to a second antigen in an individual, comprising administering to the individual an immunomodulatory polynucleotide comprising an immunostimulatory sequence (ISS) and a first antigen with a second antigen, wherein the ISS comprises the sequence 5'-cytosine, guanine-3', wherein the polynucleotide and first antigen are proximately associated, and wherein the polynucleotide and first antigen are administered in an amount sufficient to modulate an immune response in the individual to the second antigen [upon exposure to the second antigen].

4. (Amended) The method of claim [3] 1, wherein the immunomodulatory polynucleotide and first antigen are conjugated.

5. (Amended) The method of claim [3] 1, wherein the immunomodulatory polynucleotide and first antigen are proximately associated by a platform molecule.

6. (Amended) The method of claim [3] 1, wherein the immunomodulatory polynucleotide and first antigen are proximately associated by encapsulation.

11. (Amended) The method of claim 1, wherein the immunomodulatory polynucleotide and first antigen and the second antigen are administered at the same site in the individual [which is the same as the site of exposure to the second antigen].

12. (Amended) The method of claim 1, wherein the immunomodulatory polynucleotide and first antigen are administered at a site in the individual which is different from the site of [exposure to] administration of the second antigen.

22. (Amended) The method of claim 21, wherein production of second antigen-specific Th1-associated antibodies is stimulated.

25. (Amended) The method of claim [24] 1, wherein the ISS comprises the sequence 5'-TCG-3'.

26. (Amended) The method of claim [24] 1, wherein the ISS comprises the sequence 5'-purine, purine, C, G, pyrimidine, pyrimidine-3'.

37. (Amended) A [The] composition [of claim 35,] comprising

(i) an immunomodulatory polynucleotide proximately associated with a first antigen and

(ii) a second antigen,

wherein the polynucleotide comprises an immunostimulatory sequence (ISS), wherein the ISS comprises the sequence 5'-cytosine, guanine-3' and wherein the first antigen is a viral conserved polypeptide and the second antigen is a viral variable polypeptide.